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**EUROPEAN PATENT APPLICATION**

21 Application number: 79302339.1

51 Int. Cl.<sup>3</sup>: **B 01 L 3/00**  
**G 01 N 33/48**

22 Date of filing: 25.10.79

30 Priority: 23.07.79 US 59924  
25.10.78 US 954689

43 Date of publication of application:  
30.04.80 Bulletin 80/9

84 Designated Contracting States:  
AT BE CH DE FR GB IT NL SE

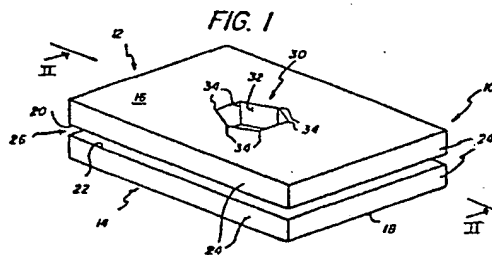
71 Applicant: EASTMAN KODAK COMPANY  
343 State Street  
Rochester, New York 14650(US)

72 Inventor: Columbus, Richard Lewis  
Kodak Park  
Rochester, New York(US)

74 Representative: Trangmar, Leigh Alan et al,  
KODAK LIMITED P.O. Box 114 246 High Holborn  
London WC1V 7EA(GB)

54 Liquid transport device.

57 A device (10) that includes an ingress aperture (30) which provides improved transport of a drop of liquid, from an exterior surface (16) of the device to the device interior. Means are provided at the intersection of the aperture sidewall (32) and the exterior surface for urging a drop deposited thereon to move into contact with the aperture sidewall and thus into the aperture. In the disclosed embodiments such means are in the form of interior corners (34).



LIQUID TRANSPORT DEVICE

This invention relates to the flow of liquid through an aperture leading from a surface, the liquid having arrived on the surface in the form of a drop.

- 5 In U.S. Patent Specification No. 3,690,836 there is disclosed a device for use in the study of chemical and biological reactions and method of making same. One embodiment therein disclosed includes an exterior surface having an aperture extending from the
- 10 exterior surface to a zone within the device. This zone is a capillary tube or chamber. The tube or chamber is filled with liquid introduced through the aperture. In this known device the ingress aperture for introduction of liquid has a smooth, cylindrical
- 15 sidewall. Such an aperture has the disadvantage that a drop of liquid which is not accurately placed on the exterior surface, that is, it is placed with its centre outside the sidewall of the aperture, tends to stay outside the aperture rather than move into it.
- 20 It is only when the centre of the drop is deposited well within the aperture that the surface tension of the liquid drop forces the drop into the aperture in full contact with the sidewall. In particular this has been a problem when the exterior surface is formed
- 25 of material which tends to be hydrophobic, that is, that forms with the liquid a liquid-vapour contact angle that is greater than  $90^\circ$ . For example certain plastics materials are sufficiently hydrophobic that drops of liquid such as blood serum are more likely to
- 30 remain on the exterior surface than to flow into the aperture.

In accordance with the present invention there is provided a liquid transport device having an exterior surface, an aperture extending from the exterior surface

35 to a zone within the device, said zone having means for

transporting the liquid through a zone, characterized in that at least the intersection of said exterior surface and the bounding surface of the aperture includes, at a predetermined location, means for  
5 substantially urging a portion of a drop of liquid deposited thereon to move into contact with the bounding surface of the aperture.

Such a device is particularly useful in introducing liquid into a transport zone between two  
10 opposed transport surfaces spaced apart a distance effective to induce capillary flow of the liquid between the transport surfaces.

Embodiments of the present invention will now be described, by way of example, with reference to  
15 the accompanying drawings in which:

Fig. 1 is an enlarged perspective view of a device in accordance with the invention;

Fig. 2 is an elevational view in section taken on the line II-II in Fig. 1, demonstrating the  
20 operation of the device;

Fig. 3 is a fragmentary, diagrammatic plan view illustrating an effect achieved in a device in accordance with the invention;

Fig. 4 is a plan view of a second embodiment  
25 of the invention; and

Fig. 5 is a sectional view taken generally along the plane of line V-V in Fig. 4.

The device and method of this invention is described in connection with embodiments featuring the  
30 capillary transport of biological liquids and particularly blood serum, between two opposed surfaces. In addition, the device and method can be applied to any liquid a drop of which is to be carried through an ingress aperture from an exterior surface to a transport means for transporting the liquid for any purpose.  
35 For example, industrial liquids can be so transported.

A device 10 constructed in accordance with one embodiment of the invention comprises (see Fig. 1) two members 12 and 14 having respective exterior surfaces 16 and 18, and respective interior, opposed surfaces 20 and 22. The members 12, 14 have boundary edge surfaces 24. Surfaces 20 and 22 are spaced apart a distance "x" (see Fig. 2) such that capillary flow of liquid is induced between the surfaces. In this manner the spaced-apart surfaces 20 and 22 define a transport zone 26 and act as means for transporting introduced liquid between the surfaces. As will be readily apparent, a range of values for "x" is permissible, and the exact value depends upon the liquid being transported.

Surfaces 20 and 22 can each be smooth, as illustrated in Figs. 1 and 2, or provided with a variety of surface configurations such as parallel grooves, the grooves of one surface being aligned, or at a positive angle, with respect to the grooves of the other.

A preferred means for introducing a drop of liquid into zone 26 is an aperture 30 extending from surface 16 to surface 20, through member 12. The aperture 30 comprises a sidewall 32 extending between the surfaces 16 and 20. The preferred largest dimension of aperture 30 in plan (for example the diameter of the smallest circle which entirely encompasses the plan form of the aperture), is one which is about equal to the greatest diameter of the drop expected to be received by the aperture 30. The drop diameter is dictated by the volume and surface tension of the drop. The volume of the drop should be adequate to fill transport zone 26 to the extent desired. For uses such as clinical analysis as herein described, a convenient drop volume is about 10  $\mu$ l. Thus, since a 10  $\mu$ l drop of serum having 70 dynes/cm surface tension

has a diameter of about 0.26 cm, the largest flow-through dimension, measured as described above is preferably about 0.26 cm.

The intersection of surface 16 and sidewall 32 is provided with means that encourage the selected drop of liquid deposited or received in the plane of surface 16 generally at aperture 30, to move into contact with the entire perimeter of sidewall 32. More specifically, sidewall 32 is shaped so as to comprise a plurality of surfaces that intersect, at least at and adjacent surface 16, at predetermined locations to form a plurality of interior corners 34. As used herein, "predetermined location" or "locations" means locations deliberately chosen, and distinguishes the present invention from cylindrical apertures which inadvertently or accidentally have imperfections, such as microscopic corners, in the sidewall. Such accidental constructs are not capable of providing the substantial urging of the drop into the aperture which the present invention provides. As shown in Fig. 1, sidewall 32 comprises throughout its perimeter, six sidewall surfaces and six such predetermined corners 34. In this embodiment equal angles of such corners 34 and equal lengths of the intersecting surfaces (measured in the direction of the perimeter of the sidewall 32) are selected to provide a shape, when viewed in plan, i.e. perpendicular to the surface 16, that is a regular hexagon, the preferred configuration.

In operation (see Fig. 2) device 10 is placed in a drop-displacing zone adjacent to a source of drops. A drop A of liquid such as blood serum, or whole blood, is dropped onto the device as a free-form drop or is touched off from a pendant surface onto surface 16 generally at aperture 30. The surface 16 preferably is maintained in a generally horizontal orientation during this step. Corners 34 act to

centre the drop and urge it into contact with the surfaces of sidewall 32. It then moves down into zone 26 and into contact with surface 22, where capillary attraction further causes the liquid to spread through-  
5 out zone 26, (see the arrows 36), so that the bounding meniscus arrives at the position shown in broken lines. Assuming sufficient volume in the drop, the spreading ceases at edge surfaces 24 which define an energy barrier to further capillary flow. Once the  
10 drop of liquid is so distributed, a variety of processing can be done to or with the liquid.

In order to ensure effective filling of the aperture the drop should be applied to aperture 30 so as to contact one of the corners. The effect is most  
15 pronounced when the centre of gravity of the drop is positioned over the aperture 30, rather than over the solid surface 16.

To vent air as the liquid advances within zone 26, means are provided within the device, such as  
20 the open space between members 12 and 14 along all or a portion of any one of edge surfaces 24. Alternatively, a second aperture (not shown) can be formed in either member 12 or 14.

The corners of the aperture 30, at the surface  
25 16 where the drop is first applied, seem to act as centres of force which induce the drop to move into contact with sidewall 32 along its entire perimeter or circumference. That is, referring to Fig. 3, it is believed that the centring force  $F_3$  of a drop A  
30 applied at one of the corners 34 is significantly greater than the corresponding centring force  $F_1$  or  $F_2$  that exists for a drop A' placed at any adjacent location 38 or 39 spaced away from a corner 34. At least one corner 34 is needed for the effect. However, at  
35 least three corners 34 are preferred, as in Fig. 3, to ensure a greater likelihood that the drop A will be in contact with a corner 34 when it contacts surface 16.

For a predetermined largest dimension of the aperture 30 calculated as described above, the greater the number of corners that are created by the use of a corresponding number of intersecting surfaces, then  
5 the greater is the likelihood that the drop will contact a corner. However, as the number of corners is increased, so is the value of the interior angle of each corner, until eventually the sidewall 32 approaches a smooth, curved surface in shape wherein all  
10 the centring forces are equal, and the effect is lost. It has been found, therefore, that a preferred number of corners is between three and about ten. Highly preferred is six corners in a regular hexagon.

As a matter of practicality, the corners 34  
15 will have a slight radius of curvature. For the corners to be effective, they each should have a radius of curvature that is no larger than about 0.4 mm.

Although flat or planar surfaces are preferred between the corners, they can also be continuously curved as is shown, between the two lower  
20 corners 34 in Fig. 3.

Although the centring mechanism of the corners is not fully understood, it is believed that the effect is due to forces that apply to the compound  
25 meniscus when the drop is located at a corner 34. As is well known, a compound meniscus is one in which the principal radii of curvature of the drop surface vary, depending on the location taken on the surface of the drop. If the drop is properly located at a corner,  
30 the compound meniscus forms a drop that extends laterally farther out over the aperture than it does when not located at a corner, and the weight of this extension causes the drop to fall or otherwise move into contact with the perimeter of sidewall 32 and  
35 then through the aperture 30. It may also be that there is at the corner a greater tendency for the drop to

wet the sidewall than would occur in the absence of a corner.

5 It will be readily appreciated that the centring force of corners 34 is needed primarily at the intersection of sidewall 32 and exterior surface 16. Thus, aperture 30 will function equally as well if sidewall 32 is smoothed out, as it approaches surface 20, to form a cylinder (not shown).

10 In addition, it will also be appreciated that the presence of a capillary zone around the downstream end of aperture 30 assists in drawing the drop through aperture 30 and into the zone.

Members 12 and 14 can be formed from any suitable material, such as plastics or metal.

15 In Figs. 4 and 5, there is illustrated a second embodiment of the device. This second embodiment is one in which a transport chamber is formed for radiometric analysis of an analyte of a biological liquid such as blood. Parts similar to those previously described bear the same reference numeral but with the distinguishing suffix "a" appended. Device 20 10a features a support member 14a (see Fig. 5), a cover member 12a, a spacer member 50 used to adhere members 12a and 14a together, and a radiometrically detectable test element 60 disposed on support 14a. The test 25 element 60 is spaced away from member 12a so that there is a transport zone 26a between element 60 and member 12a. The spacing between surface 20a and the test element 60 is such as to produce a capillary 30 effect to induce the drop that enters through aperture 30a to spread throughout the zone 26a. Preferably, the test element 60 abuts against the spacer member 50, and is held against member 14a by, for example, adhesive.

35 Thus, the members 12a, 14a and 50 define a capillary transport chamber containing the test element 60 and having any convenient shape, such as a



rectangular chamber when viewed in plan, as in Fig. 4.

Any suitable joining means can be employed between members 12a and 50, and members 50 and 14a. For example, a variety of adhesives can be used, or if  
5 all the members are thermoplastic, ultrasonic welding or heat-sealing can be used.

Member 12a is provided with an access aperture 30a extending through the member from its exterior surface 16a to zone 26a, disposed directly  
10 above a portion of test element 60. At least that portion of the aperture's sidewall 32a that intersects with surface 16a is provided with corners 34a, as described above. Preferably sidewall 32a is in the cross-sectional shape of a regular hexagon. An  
15 additional, cylindrically shaped, aperture 70 in member 12a acts as a vent for expelled air.

A viewing port 80 is optionally provided in support member 14a, particularly when the latter member is not itself transparent.

20 Test element 60 comprises an optional transparent support 62, formed, for example of poly (ethylene terephthalate), and at least an absorbent layer 64 disposed on support 62. Such layer can have a variety of binder compositions, for example,  
25 gelatin, cellulose acetate butyrate, polyvinyl alcohol, agarose and the like, the degree of hydrophilicity of which depends upon the material selected. Gelatin is particularly preferred as it acts as a wetting agent to provide for uniform liquid flow through zone 26a.  
30 Support 62 can be omitted where adequate support for layer 64 can be obtained from support member 14a.

Additional layers such as a layer 66 can be disposed above layer 64 to provide a variety of chemistries or functions, such as to provide, either  
35 in layer 66 alone or together with layer 64, a reagent composition. Filtering, registration and mordanting

functions can be provided also by such additional layers, such as are described in U.S. Patent Specification No. 4,042,335. Thus, layer 66 can comprise a reagent, such as an enzyme, and a binder of the same type as is used for layer 64.

As used herein, "reagent" in "reagent composition" means a material that is capable of interaction with an analyte, a precursor of an analyte, a decomposition product of an analyte, or an intermediate. Thus, one of the reagents can be a pre-formed, radiometrically detectable species that is caused by the analyte of choice to move out of a radiometrically opaque portion or layer of the element, such as layer 66, into a radiometrically transparent portion or layer, such as a registration layer.

The noted interaction between the reagents of the reagent composition and the analyte is therefore meant to refer to chemical reaction, catalytic activity as in the formation of an enzyme-substrate complex, or any other form of chemical or physical interaction, including physical displacement, that can produce ultimately a radiometrically detectable signal in the element 60. As is well known, radiometric detection includes both colorimetric and fluorimetric detection, depending upon the indicator reagent selected for the assay. The assay of the element is designed to produce a signal that is proportional to the amount of analyte that is present.

A wide variety of radiometric assays can be provided by element 60. Preferably, the assays are all oxygen-independent, as the flow of blood or blood serum into zone 26a tends to seal off element 60 from any additional oxygen. Typical analytes which can be tested include BUN, total protein, bilirubin and the like. The necessary reagents and binder or vehicle compositions for the layers of element 60, such as

layers 64 and 66, for these analytes can be those described in, respectively, U.S. Patent Specification Nos. 4,066,403, 4,132,528 and 4,069,016 or 4,069,017.

Quantitative detection of the change produced in element 60 by reason of the analyte of the test element is preferably made by scanning the element through port 80 with a photometer or fluorimeter. A variety of such instruments can be used, for example the radiometer disclosed in German OLS 2,755,334, or the photometer described in U.S. Patent Specification No. 4,119,381.

The following is an illustrative example of the device shown in Figs. 4 and 5.

Example

Members 12a and 14a are formed from polystyrene of a thickness 0.127 and 0.254 mm, respectively. Member 50 is steel of a thickness 0.38 mm. The three members are sealed together by adhesives such as polybutyl acrylate adhesive obtainable from Franklin Chemical under the trademark "Covinax". Apertures 30a and 70 in member 12a are about 8 mm apart on centre. The outside diameter of the hexagon form of aperture 30a is about 2.6 mm. View port 80 is about 5 mm in diameter. The capillary spacing between test element 60 and member 12a is about 0.05 mm and the width of element 60 is about 11.5 mm.

For a test element 60 designed to detect total protein in a 10  $\mu$ l drop of blood serum, the following sequential layers are used:

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| <u>Layer</u> | <u>Composition</u>                        | <u>Amount</u>         |
|--------------|---|-----------------------|
| 62           | Gelatin-subbed                            | 175 microns           |
|              | poly(ethylene terephthalate)              | thick                 |
| 5            | poly(acrylamide-co-N-vinyl-2-pyrrolidone) | 16.0 g/m <sup>2</sup> |
| 64           | CuSO <sub>4</sub> ·5H <sub>2</sub> O      | 10.8 g/m <sup>2</sup> |
|              | LiOH                                      | 5.4 g/m <sup>2</sup>  |
|              | tartaric acid                             | 8.0 g/m <sup>2</sup>  |

CLAIMS

1. A liquid transport device having an exterior surface, an aperture extending from the exterior surface to a zone within the device, said zone having means for transporting the liquid through a zone, characterized in that at least the intersection of said exterior surface and the bounding surface of the aperture includes, at a predetermined location, means for substantially urging a portion of a drop of liquid deposited thereon to move into contact with the bounding surface of the aperture.
2. A device according to claim 1, characterized in that said urging means comprises a surface configuration capable of forming a compound meniscus on a contacting liquid drop.
3. A device according to claim 1 or 2, characterized in that said urging means comprises at least one interior corner in the bounding surface of the aperture at at least its intersection with said exterior surface.
4. A device according to claim 3, characterized in that there are from three to ten similar interior corners at predetermined spaced-apart locations at at least said intersection.
5. A device according to claim 4, characterized in that there are six of said corners.
6. A device according to claim 5, characterized in that the bounding surface of the aperture conforms to a regular hexagon at least adjacent the exterior surface.
7. A device according to any one of the preceding claims, characterized in that the transporting means in said zone includes two opposed surfaces of the zone spaced apart a distance such as to cause capillarity.

8. A device according to claim 7, characterized in that at least one of said two spaced-apart opposed surfaces includes an absorbent layer containing at least one reagent capable of producing a  
5 radiometrically detectable signal when contacted by the liquid of the drop.

9. A device according to claim 3 or any one of claims 4 to 8 when appendant directly or indirectly to claim 3, characterized in that the  
10 corner or each of the corners extends throughout the length of the bounding surface of the aperture, from the exterior surface to the zone.

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FIG. 1

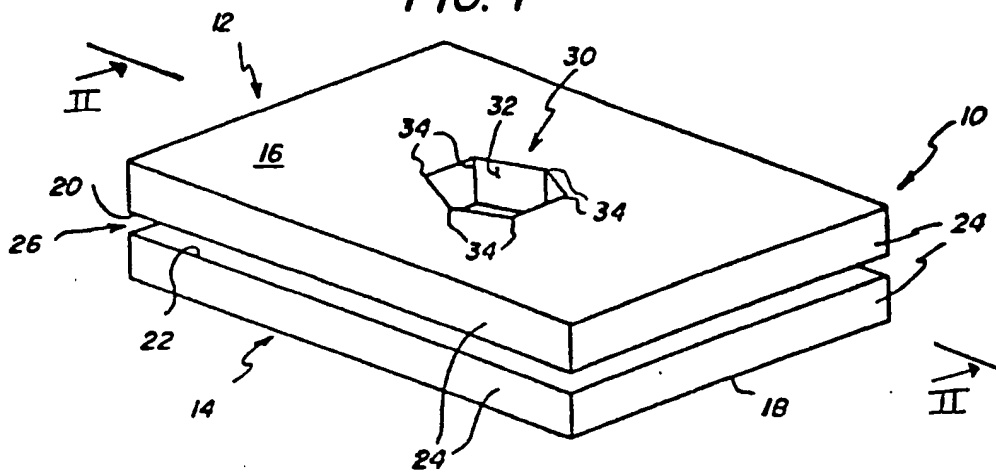


FIG. 2

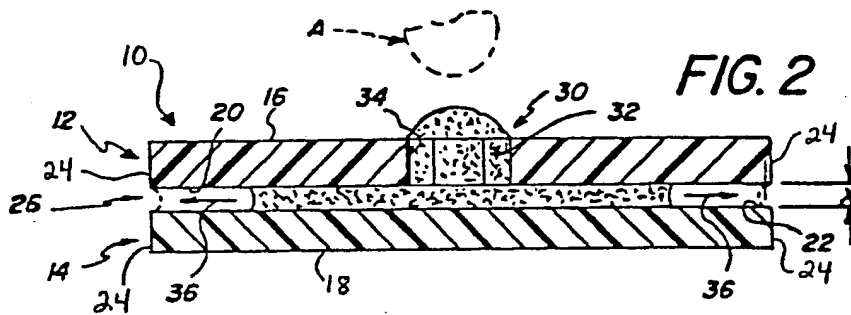


FIG. 3

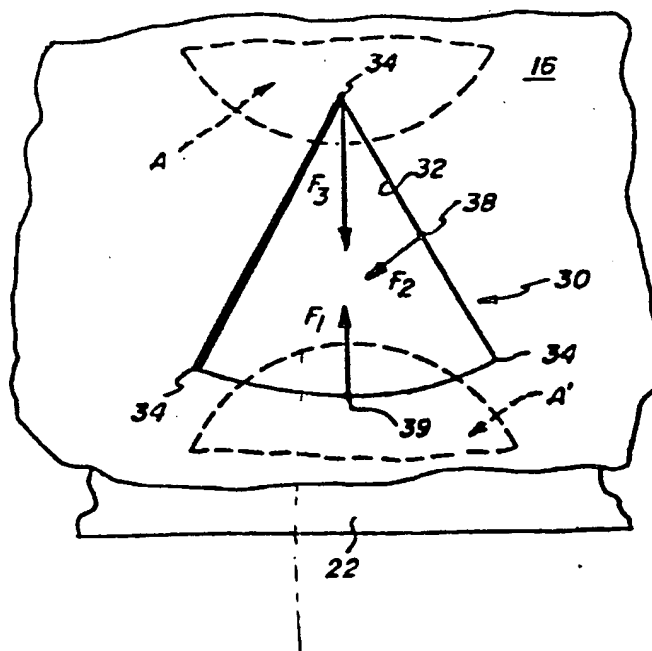


FIG. 4

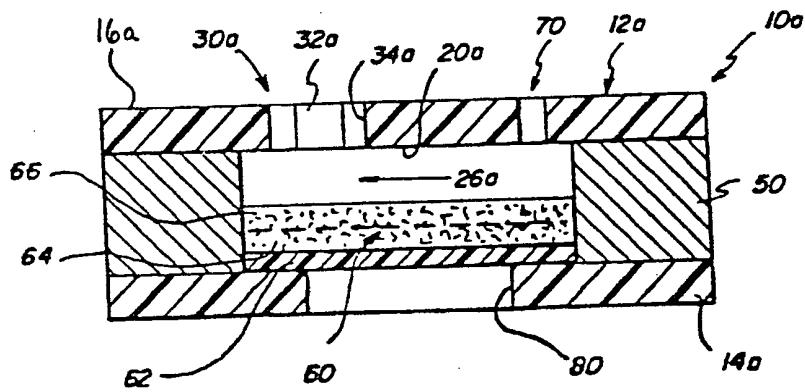
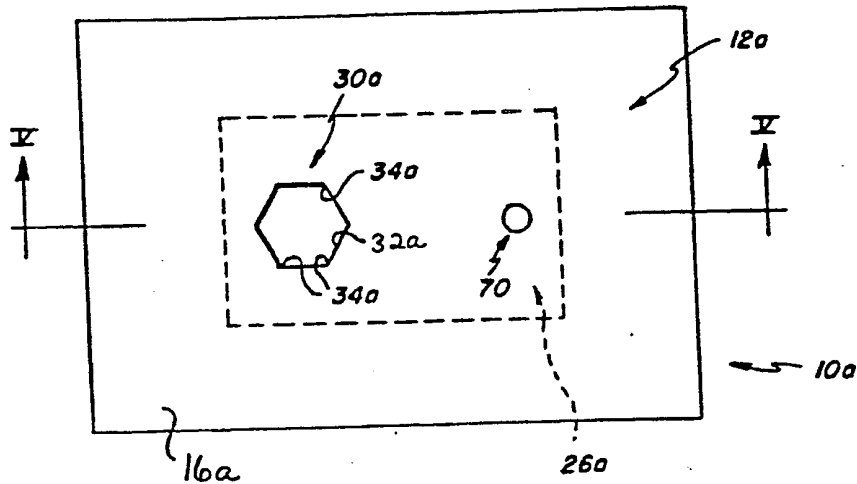


FIG. 5





European Patent  
Office

# EUROPEAN SEARCH REPORT

0010456  
Application number

EP 79 30 2339

| DOCUMENTS CONSIDERED TO BE RELEVANT  |   |  | CLASSIFICATION OF THE APPLICATION (Int. Cl. 3)  |
|--|---|--|---|
| Category   | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim                              |   |
| D  | <u>US - A - 3 690 836</u> (J. BUISSIERE)<br>* Whole document *                | 1  | B 01 L 3/00<br>G 01 N 33/48   |
| A  | <u>FR - A - 1 444 146</u> (PROMOVEO)<br>* Whole document *                    | 1  |   |
| A  | <u>US - A - 3 565 537</u> (J. FIELDING)<br>* Whole document *                 | 1  |   |
| A  | <u>US - A - 3 992 158</u> (E.P. PRZYBYLO-WICZ)<br>* Whole document *          | 1  | TECHNICAL FIELDS SEARCHED (Int.Cl. 3)<br><br>B 01 L 3/00<br>G 01 N 33/48<br>21/29   |
|  |   |  | CATEGORY OF CITED DOCUMENTS<br><br>X: particularly relevant<br>A: technological background<br>O: non-written disclosure<br>P: intermediate document<br>T: theory or principle underlying the invention<br>E: conflicting application<br>D: document cited in the application<br>L: citation for other reasons |
| <input checked="" type="checkbox"/> The present search report has been drawn up for all claims |   |  | S: member of the same patent family, corresponding document   |
| Place of search<br>The Hague   |   | Date of completion of the search<br>31-01-1980 | Examiner<br>DUCHATELLIER  |

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